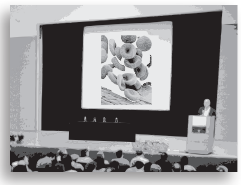
News

Conference Scene



Nanoparticles prove successful at clotting blood

According to a study published in the December issue of the *Science Translational Medicine* journal, researchers at Case Western University, Cleveland (OH, USA) have manufactured an entirely synthetic blood clotting agent. The synthetic particles stick to platelets in the body and exhibit greater blood clotting capabilities than drugs (i.e., NovoSeven) currently used to facilitate the coagulation process following traumatic injury.

Using Arg–Gly–Asp functionalized nanoparticles, Erin Lavik and her team at Case Western developed synthetic platelets capable of halving the bleeding time (from ~4 to 2 min) following intravenous injection in rodent models with severed femoral arteries. At a dose of 20 mg/ml, the synthetic particles cleared within 24 h and no adverse side effects were seen within 7 days post-infusion. Fluorescently labeled versions of the synthetic particles permitted the assessment of nanoparticle retention and accumulation in noninjured tissues – a risk factor for unwanted and dangerous clotting. No such accumulate was detected.

Polythene glycol (PEG) surrounds the polymer core of each nanoparticle and through its solubility in water prevents them sticking to one another and blood vessels. A protein sequence that platelets have previously been shown to bind to was positioned atop these PEG molecules – "people had previously shown that activated platelets bind to [this sequence], so we optimized the chemistry to expose the molecule, presenting them to activated platelets," commented Lavik.

An established avenue of investigation, blood platelet mimics have been engineered before, however "those particles can build up in capillary beds, increasing the potential for [dangerous blood clots]", explained Lavik. With collaborator James Bertram, a graduate student at Yale, Lavik's synthetic particle – approximately a third of the size of normal platelets – is capable of flowing within capillaries and exhibiting platelet-specific stickiness.

Thinking ahead, Lavik commented on potential collaboration between NovoSeven and her nanoparticles in traumatic injury treatment due to their potentially complementary modes of action. Interestingly, NovoSeven "works to help build the fibrin mesh network that's critical in building clot. Perhaps the synthetic platelets could help start building the clot and the drug might help stabilize it", explained Lavik.

Discussing the potential applications of Lavik's synthetic particles, John Weisel, a researcher at Penn Medical School, commented on "the potential [for the nanoparticles] to be useful for controlling bleeding on the battlefield."

Future research will investigate the efficacy of these particles in blood clotting in animals with circulatory systems more representative of that in humans. "The early research looks very promising, but the human system is different than a rat's," mentioned Rutledge Ellis-Behnke, a researcher at Massachusettes Institute of Technology (MA, USA). "Care has to be taken that these do not coat the inside of the lungs and reduce the amount of oxygen transfer into red blood cells." Exploration into the applicability of these particles to different forms of traumatic injury is also required.

Sources: Technology Review published by MIT Review: Synthetics Stop the Bleeding: www.technologyreview.com; Bertram JP, Williams CA, Robinson R et al. *Intravenous hemostat: nanotechnology to halt bleeding.* Sci. Transl. Med. *1(11) 11–22 (2009).*

> *"...Lavik's synthetic particle – approximately a third of the size of normal platelets – is capable of flowing within capillaries and exhibiting platelet-specific stickiness."*

future medicine part of fsg

Rapid nanosensor device to detect biomarkers in whole blood

"*When exposed to blood, the chip effectively concentrates the biomarkers by capturing them while the rest of the blood is washed away, allowing detection at very low concentrations.*"

Scientists at Yale, Cornell and Harvard Universities (USA) have for the first time used label-free nanosensors to detect cancer biomarkers in whole blood. The sensitive and rapid technology could have a high potential in a clinical setting for cancer biomarker detection.

Whole blood is a complex solution, with traditional nanosensors encountering problems including non-specific binding and biofouling (the accumulation of unwanted substances). High concentrations of biomarkers are required for efficient detection. To overcome these limitations, the researchers used a microfluidic purification chip ahead of the nanosensor, separating the process into two stages – purification and detection.

Current biomarker tests using whole blood are labor-intensive, with the need for a controlled laboratory setting and a centrifuge to separate blood components. The recently published research allowed detection of two model cancer antigens (prostate and breast cancer) in less than 20 min.

The microfluidic chip, on which disease-specific antibodies are attached, acts as a filter. When exposed to blood, the chip effectively concentrates the biomarkers by capturing them while the rest of the blood is washed away, allowing detection at very low concentrations. The antibody–biomarker complex is cleaved from the chip and measured using a detector.

Tarek Fahmy, Associate Professor of Biomedical Engineering & Chemical Engineering (Yale University, CT, USA) highlighted the clinical applications of these devices, "Doctors could have these small, portable devices in their offices and get nearly instant readings. They could also carry them into the field and test patients on site."

The future potential applications include the ability to simultaneously test for a wide range of biomarkers in blood, and the possibility of testing other complex biological fluids. Associate Director of the Yale Institute for Nanoscience and Quantum Engineering, Mark Reed, who led the team, commented on the research: "The advantage of this technology is that it takes the same effort to make a million devices as it does to make just one. We've brought the power of modern microelectronics to cancer detection."

Sources: Stern E, Vacic A, Rajan NK et al.*: Label-free biomarker detection from whole blood.* Nat. Nanotechnol. *DOI: 10.1038/nnano.2009.353 (2009) (Epub ahead of print).*

Color-changing contact lenses indicate blood glucose level in diabetes

Diabetics may soon be able to wear contact lenses that continuously alert them to variations in their glucose levels by changing colors, replacing the need to routinely draw blood throughout the day.

The noninvasive technology, developed by Chemical and Biochemical Engineering professor Jin Zhang at The University of Western Ontario, uses extremely small nanoparticles embedded into the hydrogel lenses. The engineered nanoparticles react with glucose molecules found in tears, causing a chemical reaction that changes their color.

Zhang has received US$216,342 in total from the Canada Foundation for Innovation to further develop technologies using multifunctional nanocomposites, which can be used for a range of other applications outside of ophthalmological technology and biomedical devices.

Source: University of Western Ontario, ON, Canada

Small soldiers combine arms to go to war on tumor cells

Nanotechnology offers great hope for the future treatment of cancer. However, there remain a number of stumbling blocks that must be cleared before this hope becomes a reality. One of these challenges is to design molecules that are capable of both remaining in the circulation for long enough to encounter the tumor and of killing the tumor cells when they get there.

A team of chemists from the University of California (UC), San Diego (USA), cell biologists from UC Santa Monica and bioengineers from the Koch Institute for Integrative Cancer Research at MIT have designed an innovative two-part system to tackle this problem, whereby nanoparticles designed to locate the tumor cells were injected first, followed by a second particle designed to kill those cells. The team's findings have been published online in the *Proceedings of the National Academy of Sciences*.

Sangeeta Bhatia of MIT (MA, USA) clarified the problem, "A nanoparticle that is engineered to circulate through a cancer patient's body for a long period of time is more likely to encounter a tumor. However, that nanoparticle may not be able to stick to tumor cells once it finds them. Likewise, a particle that is engineered to adhere tightly to tumors may not be able to circulate in the body long enough to encounter one in the first place."

The team attempted to circumvent this problem by using two different particles – a gold nanorod 'activator' and a 'responder', consisting of either iron oxide nanoworms or liposomal doxorubicin. The activator is injected first and accumulates in the tumor owing to the tumor's leaky vasculature, eventually covering the entire tumor. After 3 days these gold nanorods are then heated by a weak, and otherwise benign, infrared laser, sensitizing the tumor. Finally, the responder, coated with a molecule specific for the heat-treated tumor, is administered.

"Think of them like soldiers attacking an enemy base," explained primary author Michael Sailor, of UC San Diego. "The gold nanorods are the Special Forces, who come in first to mark the target. Then the Air Force flies in to deliver the laser-guided bomb. The devices are designed to minimize collateral damage to the rest of the body."

The two responders have distinct properties that would make them useful in the clinic. The iron oxide nanoworms are visible on MRI whilst the liposomal doxorubicin was demonstrated to arrest and then shrink tumors in live mice.

"The nanoworms would be useful to help the medical team identify the size and shape of a tumor in a patient before surgery, while the hollow nanoparticles might be used to kill the tumor without the need for surgery," said Sailor.

"This study is important because it is the first example of a combined, two-part nanosystem that can produce sustained reduction in tumor volume in live animals," He concluded.

Source: Park J-H, von Maltzahn G, Xu MJ et al. *Cooperative nanomaterial system to sensitize, target, and treat tumors.* Proc. Natl Acad. Sci. USA *107(3) 981–986 (2010).*

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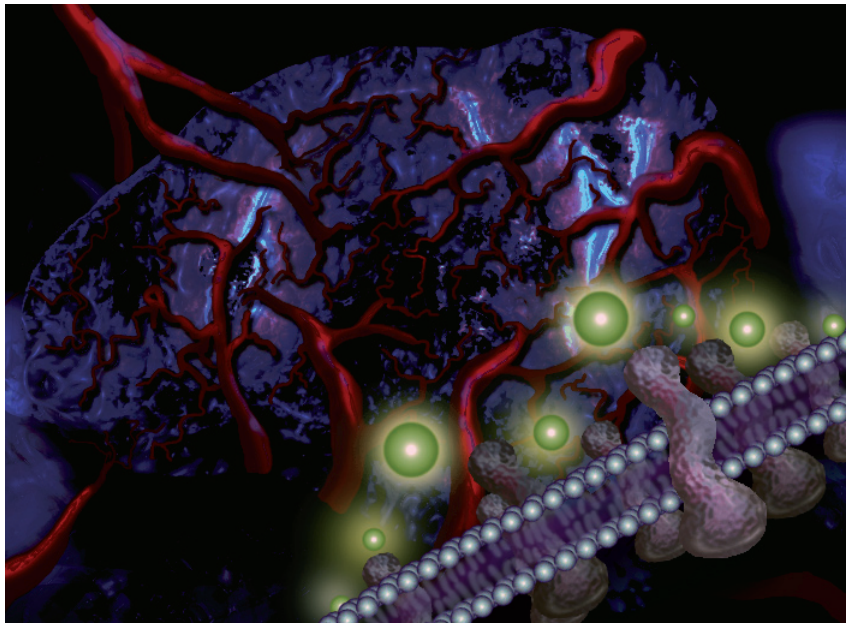

About the News

The News highlights some of the most important events and research in the field of nanomedicine. If you have newsworthy information, please contact: Morag Robertson, Commissioning Editor, *Nanomedicine*; m.robertson@future-science.com